



Group Art Unit: 1624

Examiner: McKenzie, T.

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Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

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- CERTIFICATE OF MAILING**
(37 C.F.R. §1.8a)

Kimila Carraway
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The Commissioner is authorized to charge any fee required, or to credit any overpayment, to our Deposit Account No. **50-2613**.

Respectfully submitted,

Dated: 2/25/04

By: *Diana L. Bush*
Diana L. Bush, Ph.D., Esq.
Reg. No. 51,109

PAUL, HASTINGS, JANOFSKY & WALKER LLP
3579 Valley Centre Drive
San Diego, CA 92130-2081
Phone: (858) 720-2500
Fax: (858) 720-2555



Patent
45198.00013.RCE (CIP1)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erion *et al.*

Serial No.: 09/518,501

Filed: March 3, 2000

Title: NOVEL PHOSPHORUS-CONTAINING
PRODRUGS

Group Art Unit: 1624

Examiner: McKenzie, T.

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In compliance with Applicants' duty under 37 CFR 1.56, the following information is brought to the attention of the Examiner. The items are listed on the attached Form PTO/SB/08A and copies are enclosed for the convenience of the Examiner. Applicants respectfully request that the documents be made of record in the above-referenced application. Applicants also request that the Examiner return an initialed copy of the attached Form PTO/SB/08A with the next Official Action indicating that the documents have been considered.

The items identified in this Supplemental Information Disclosure Statement may or may not be "material" pursuant to 37 CFR 1.56 and the submission thereof by Applicants shall not be construed as an

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I hereby certify that this paper (along with anything referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as First Class Mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450

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Supplemental Information Disclosure Statement

Serial No.: 09/518,501

Page 2 of 2

admission that any such patent, publication or other information referred to therein is material or considered to be material (37 CFR 1.97(h)), or even qualifies as "prior art" under 35 U.S.C. § 102 with respect to this invention unless specifically designated by Applicants as such.

The filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information, as defined in 37 CFR 1.56, exists.

This Supplemental Information Disclosure Statement is being submitted under 37 CFR 1.97(c)(2). Enclosed is a check including the amount of \$180.00 to cover the fee pursuant to 37 CFR 1.17(p). However, if counsel for Applicants is in error in this regard, the Commissioner is authorized to charge any additional fee, or to credit any overpayment, to Deposit Account No. **50-2613**.

Respectfully submitted,

Dated: 2/25/04

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Diana L. Bush, Ph.D., Esq.
Reg. No. 51,109

Paul, Hastings, Janofsky & Walker LLP
3579 Valley Centre Drive
San Diego, CA 92130
Direct Dial: (858) 720-2885
Facsimile: (858) 720-2555

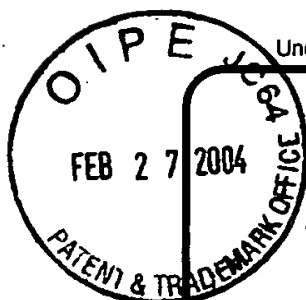
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 3

Complete if Known

Application Number	09/518,501
Filing Date	March 3, 2000
First Named Inventor	Erion et al.
Group Art Unit	1624
Examiner Name	T. McKenzie
Attorney Docket Number	032465.00013.RCE (CIP1)

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

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NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Beaucage and Iyer, "The Synthesis of Modified Oligonucleotides by the Phosphoramidite Approach and Their Applications," <u>Tetrahedron</u> , 49(28):6123-6194 (1993).	
		Borch and Millard, "The Mechanism of Activation of 4-Hydroxycyclophosphamide," <u>J. Med. Chem.</u> , 30:427-431 (1987).	
		Cooper et al., "Use of Carbohydrate Derivatives for Studies of Phosphorus Stereo-chemistry. Part II. Synthesis and Configurational Assignments of 1,3,2-Oxathiaphosphorinan-2-ones and 1,3,2-Dioxaphosphorinan-2-thiones," <u>J. Chem. Soc., Perk. Trans. 1</u> , (10):1049-1052 (1974).	
		De Clercq et al., "A Novel Selective Broad-spectrum Anti-DNA Virus Agent," <u>Nature</u> , 323:464-467 (1986).	
		Farquhar et al., "Synthesis and Antitumor Evaluation of Bis[(pivaloyloxy)methyl] 2'-Deoxy-5-fluorouridine 5'-Monophosphate (FdUMP): A Strategy to Introduce Nucleotides into Cells," <u>J. Med. Chem.</u> , 37:3902-3909 (1994).	

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¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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		Friis and Bundgaard, "Prodrugs of Phosphates and Phosphonates: Novel Lipophilic α -acyloxyalkyl Ester Derivatives of Phosphate- or Phosphonate Containing Drugs Masking the Negative Charges of these Groups," <u>Euro. J. Pharm. Sci.</u> , 4:49-59 (1996).	
		Harada et al., "Resolution of 1,3-alkanediols Via Chiral Spiroketal Derived from ι -Menthone," <u>Tetrahedron</u> , 28(41):4843-4846 (1987).	
		Khorana et al., "Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters," <u>JACS</u> , 79:430-436 (1957).	
		Korba et al., "Liver-targeted Antiviral Nucleosides: Enhanced Antiviral Activity of Phosphatidyl-dideoxyguanosine Versus Dideoxyguanosine in Woodchuck Hepatitis Virus Infection <i>In Vivo</i> ," <u>Hepatology</u> , 23(5):958-963 (1996).	
		Lefebvre et al., "Mononucleoside Phosphotriester Derivatives with <i>S</i> -acyl-2-thioethyl Bioreversible Phosphate-protecting Groups: Intracellular Delivery of 3'azido-2',3'dideoxythymidine 5'-monophosphate," <u>J. Med. Chem.</u> , 38:3941-3950 (1995).	
		Ludeman et al., "Synthesis and Antitumor Activity of Cyclophosphamide Analogues. 4. Preparation, Kinetic Studies, and Anticancer Screening of "Phenylketophosphamide" and Similar Compounds Related to the Cyclophosphamide Metabolite Aldophosphamide," <u>J. Med. Chem.</u> , 29:716-727 (1986).	
		McGuigan et al., "Intracellular Delivery of Bioactive AZT Nucleotides by Aryl Phosphate Derivatives of AZT," <u>J. Med. Chem.</u> , 36:1048-1052 (1993).	
		Mosbo and Verkade, "Dipole Moment, Nuclear Magnetic Resonance, and Infrared Studies of Phosphorus Configurations and Equilibria in 2-R-2-Oxo-1,3,2-dioxaphosphorinanes," <u>J. Org. Chem.</u> , 42(9):1549-1555 (1977).	
		Nakayama and Thompson, "A Highly Enantioselective Synthesis of Phosphate Triesters," <u>J. Am. Chem. Soc.</u> , 112:6936-3942 (1990).	
		Ramachandran et al., "Efficient General Synthesis of 1,2- and 1,3-diols in High Enantiomeric Excess via the Intramolecular Asymmetric Reduction of the Corresponding Ketoalkyl Diisopinocampheylborinate Intermediates," <u>Tetrahedron</u> , 38(5):761-764 (1997).	

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Sheet 3 of 3

Application Number 09/518,501
Filing Date March 3, 2000
First Named Inventor Erion et al.
Group Art Unit 1624
Examiner Name T. McKenzie
Attorney Docket Number 032465.00013.RCE (CIP1)

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		Starrett, Jr. et al., "Synthesis, Oral Bioavailability Determination, and <i>in Vitro</i> Evaluation of Prodrugs of the Antiviral Agent 9-[2-(Phosphonomethoxy)ethyl]adenine (PMEA)," <u>J. Med. Chem.</u> , 37:1857-1864 (1994).	
		Thomson et al., "Synthesis, Bioactivation and Anti-HIV Activity of the Bis(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Esters of the 5'-monophosphate of AZT," <u>J. Chem. Soc., Perk. Trans. 1</u> , (11):1239-1245 (1993).	
		Weber and Waxman, "Activation of the Anti-cancer Drug Ifosfamide by Rat Liver Microsomal P450 Enzymes," <u>Biochem. Pharm.</u> , 45(8):1685-1694 (1993).	
		Zon et al., "NMR Spectroscopic Studies of Intermediary Metabolites of Cyclophosphamide. A Comprehensive Kinetic Analysis of the Interconversion of <i>cis</i> - and <i>trans</i> -4-Hydroxycyclophosphamide with Aldophosphamide and Concomitant Partitioning of Aldophosphamide Between Irreversible Fragmentation and Reversible Conjugation Pathways," <u>J. Med. Chem.</u> 27:466-485 (1984).	

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